

A Review on Technology Development and Transfer

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ABSTRACT:

In the present scenario, interest in profiting from an industry's technological assets through technology transfer has been boosted. Technology Transfer is defined as a "logical process that manages the transfer of any process with its documentation and professional moxie between developments or manufacture sites". Technology Transfer is integral and significant to drug discovery and development methods for brand-new healthful medicinal products. This method provides necessary data for technology transfer from R&D to the PDL/F&D/MS&T Department and expansion of existing products to the assembly for exploitation or commercialization. Also, to assure the drug quality, safety and efficacy, it's desired to ensure positive five W's and one H, that is, what, when and why data should be transferred to wherever and by whom and the way (how) to move, then share information and knowledge of the technology transfer between stakeholders related to drug producing. The article attempts to debate the technology transfer process, the steps involved in technology transfer, reasons for using technology Transfer, the importance of technology transfer and also the issues involved in the technology transfer within the pharmaceutical industry.

KEYWORDS: Technology transfer, Scale-up, Exhibit, Pharmaceutical production.

I. INTRODUCTION:

Technology transfer is the process of moving technology from one Entity to another. World Intellectual property Organization (WIPO) defines "A series of operations for transferring ideas, knowledge, technology and Skills with another individual or institution (E.g., a Company, a university or a governmental body) and of accession of similar ideas, Knowledge technologies and Skills by others. Technology transfer is transferring scientific findings from one association to another for more evolution. Consequently, new

products like medicines, educational tools, electronic devices, security equipment and health services can be accessible to the public. Technology transfer is the junction between business, science, engineering, law and Government. In recent times, there is a growing consciousness that a proper transfer of manufacturing technologies (technology transfer) is important to upgrade medicine quality as aimed during R&D to be a final product, during manufacture as well as reassure stable quality transferred for numerous reasons between the contract giver and contract acceptor during manufacture. Technology transfer requires a planned approach utilizing trained and knowledgeable staff working within a robust quality system, with data documentation covering all production and quality control aspects. For that purpose, it is necessary to establish a suitable process that categorizes information generated in the processes through pharmaceutical R&D and manufacturing as well as the information flows, discusses information required for the technology transfer and Communication route and proposes ideal technological transfer. [2,5,13]

MAIN TEXT

GENERAL PRINCIPLES OF TECHNOLOGY TRANSFER (TT)

The introductory or necessities of Technology Transfer are:^[1]

- Quality Risk Management (QRM)
- Documented approach
- Logical approach
- Sending Unit (SU)
- Receiving Unit (RU)
- Skillful and Professional personnel

The following general principles are to be deployed for a successful TT:^[1]

- The project should achieve the quality parameters based on QRM.

- The installations and equipment present in SU and RU should be the same.
- Professional and skilful personnel should be available at RU.
- RU should produce documented evidence of the transferred product, method or manufacturing method against the predetermined specifications of SU.
- Reporting of faulty specifications outcome and miscalculation by the RU to SU
- The certainty of the transfer process should be preserved.
- The legal intimations like royalties, intellectual property rights (IPR), and competing interests should be conveyed earlier and during the transfer.

TECHNOLOGY TRANSFER PROTOCOLS

SU, RU should control the transfer process and, if needed, an additional agency in which conventional directions and approvals are provided. A simple management plan and formal agreements should exist for successful technology transfer.^[1]

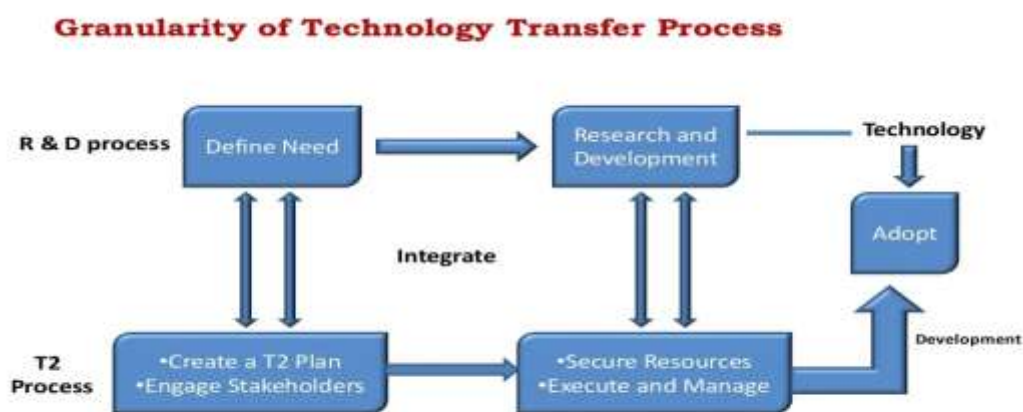
The following measures should be followed as per the transfer protocol.^[1]

- Purpose and aim of the transfer.
- Extent of the transfer.
- Professional personnel and their responsibilities.
- Comparison of information, equipment and processes between SU and RU.
- Documented proof of each stage of process control and critical stages.

- The transfer of documents should be attained satisfactorily.
- Assessment of CCP (critical control points).
- Assessment of experimental method for production.
- Experimental process assessment for standardization and analysis.
- Details of individual batches.
- Process validation.
- Evaluation of specification or deprived results and change control.
- Analysis of finished products.
- Attested reports of analysis.
- Retention of reference materials, active pharmaceutical ingredients (API), and intermediate and finished products.
- Approval of concerned authorities or project manager.

Information Required For Technology Transfer^[1]

For the successful technology transfer from the R&D section to production, the RU should have the potential to perform and accommodate the production capacity. The detailed method development should be transferred. At RU, expert staff and facilities accessible at the site are the primary considerations. A protocol development by SU and RU is necessary for the technology transfer.



Granularity: The scale or level of detail in a set of data.

Fig. 1 Granularity of Technology Transfer Process

1 Starting Materials: For successful technology transfer to production, the specifications of starting materials like API and excipients should be identical at SU and RU.

a. Active Pharmaceutical Ingredients (API): The sending Unit (SU) should offer the Receiving Unit (RU) with the open (Applicants) Active Substance Master File (ASMF), or Drug Master File (DMF) or API master file (APIMF) and any essential supplement data on an API suitable for manufacturing of pharmaceutical products.

Some of the vital information is mentioned below: -

- Details of API manufacturer and supplier.
- Detail synthesis scheme, process outline, raw materials, and process control.
- Details of intermediate products.
- Complete information on API for the formulation process. It includes:
 - Physicochemical parameters like solubility and partition coefficient (method of determination).
 - Particle size distribution.
 - Bulk and tap density with the exact method of evaluation.
 - Disintegration profile.
 - Nature of hygroscopicity.
 - Water content.
 - Loss on drying.
 - Limit impurities.
- Microbiological factors.
- Environmental factors.
- Pharmacopeial standards with a method of determination.
- Stability studies.
- Storage and handling guidance mentioned in Pharmacopoeias.

b. Excipients: The excipients used in manufacturing have an essential role in the quality of the finished product. SU has to provide detailed information on excipients to RU. The following information is some examples of complex data:

- Solubility
- Category of excipients.
- Dosage forms available.
- Descriptions.
- Details of manufacturer and supplier.
- For transdermal dosage form:
 - (a) Particle size and distribution
 - (b) Lipophilicity, Partition coefficient
 - (c) Dissolution rate with detailed process
 - (d) Water content and loss of drying
 - (e) Specific gravity
- For solid dosage form:
 - (a) Particle size and distribution

(b) Bulk and tap density profile with a detailed method of evaluation

- (c) Compaction properties
- (d) Water content and loss of drying
- (e) Nature of hygroscopicity

• For semi-solid dosage form:

- (a) Melting point
- (b) Range of pH
- (c) Viscosity
- (d) Specific gravity

• For liquid dosage form:

- (a) Range of pH
- (b) Viscosity
- (c) Specific gravity
- (d) Water content

• For parenteral formulation:

- (a) Range of pH
- (b) Viscosity
- (c) Specific gravity
- (d) Water content

(e) Osmotic pressure

• For aerosol/inhaled dosage form:

- (a) Solubility
- (b) Bulk and tap density
- (c) Particle size and distribution
- (d) Surface area

Process Information ^[1]

Regarding the information on the process and testing, the SU should provide the following information.

- (a) Requirement of the facility.
- (b) Requirement of equipment.
- (c) Requirement of a skilled person.
- (d) Storage guidelines and handling of raw materials and finished goods.
- (e) Detail information on raw materials.
- (f) Availability of all SOPs.
- (g) Manufacturing process.

- Process optimization
- Process flow charts
- Environmental factors.
- Reaction conditions
- Details of intermediate products
- Detail master batch records

(h) Analytical methods

- Assay procedure
- Standardization process
- Finished products testing

(i) Validation protocols

- Equipment validation
- Process validation

(j) Change control, critical control point and corrective actions.

- (k) Annual audits and reviews
- (l) Quality control and Quality assurance.

3 Finished Products

A finished pharmaceutical product (FPP) is a final product that has undergone all production and manufacturing stages. The final product should be stored in a specific container, and proper labelling is compulsory. All the information, in a well-documented form, should be transferred from SU to RU. The finished product storage and handling guidelines will be reported to RU, along with the analytical test procedure and accurate specification. The pre-established specifications should be analysed, and the thorough standardization process should be transferred.^[1]

4 Packaging^[1]

Data regarding the packaging of the finished product should be transferred to RU. Some of the necessary instructions are given below:

- Suitable container
- Proper closure system
- Packing material
- Process of packaging
- Design of packaging
- Proper labelling
- Relevant information mentioned in the package and label.

The information provided by SU should be checked at RU for packaging, whether the packaging is safe, suitable, protective and compatible with the finished product. Packaging should be suggested so that the finished product is not affected by environmental factors or decomposed. The product should be protected from sunlight and should not be oxidized. The development of unwanted substances can make the product toxic and spurious. The container shouldn't react with the product, and the effectiveness of the product should not be altered by any means after packaging.^[1]

5 Documentation^[1]

Some of the essential documents required in technology transfer are:

- Technology transfer protocol, qualification protocol and report.
- Training protocols and reports.
- Standard Operating Procedure (SOP).
- Technology transfer report.
- Analytical methods transfer protocol.
- Validation report (VR).
- Process validation report.

- Cleaning validation protocol and report.
- Validation Master Plan (VMP).
- Master batch record.

For a successful T2, the documents related to the facility available at RU, a detailed illustration of the manufacturing method, sampling procedures, approved SOPs for all equipment and processes, information on packaging, storage, stability information, cleaning, validations, and regulatory needs should be supplied by SU to RU before initiating the productions.^[1]

6 Premises

The SU should provide data regarding the layout and construction of buildings and facilities. The ventilation, air-conditioning system, temperature, humidity, and compressed air-related data should be provided to RU before production. RU should include the safety requirements, risk management, waste management provisions and emergency protocols in the list of data.^[1]

7 Equipment^[1]

The SU should supply the following to RU regarding equipment:

- List of equipment required.
- Specific models and makers of equipment.
- Manuals and SOPs.
- Set-up, maintenance, calibration and storage protocol.
- IQ, OQ and PQ status.

8 Qualification and Validation

The qualification and validation protocol should be determined based on QRM (Quality Risk Management) and provided by SU to RU in a well-attested manner.^[1]

9 Analytical Method Transfer^[1]

Analytical methods analysed raw materials, finished products, cleaning samples and packaging materials. Analytical method transfer should be executed by providing all the data regarding analytical testing. The SU should provide the following details for analytical method transfer:

- The methods of analysing and testing raw materials and finished products.
- Training for analysts and staff.
- Details of equipment used for the testing.
- Quality control testing results.
- Experimental principle, design and methods.
- Testing parameters.
- Validation reports.

After getting all data from the Sending Unit, the Receiving Unit should have some responsibilities for the successful analytical transfer, which is

- Agreement in acceptance criteria.
- Review of analytical methods.
- Trained and skilled staff.
- Availability of necessary equipment.
- Execution of transfer protocol.
- Documents for recording the analytical results.
- Availability of Pharmacopoeias.
- Proper validation to implement the process.

WHO has referred to the possible experimental designs for analytical testing. The tests are:

- Identification test.
- Content uniformity.
- Solubility.
- Assay or percentage purity of the components.
- Dissolution parameter.
- Qualitative and quantitative tests for microbiological assays.
- Limit test for impurities.
- Residues recovery.

The responsibilities of both SU and RU should be performed and prepare the report jointly to execute the transfer protocol.

Sr. No.	Responsibilities of Team Member	Responsibilities of Team Member
1	Process Technology	The central focus for transfer activities, aggregate documentation from donor site, performs initial assessment of transferred project for feasibility, compatibility with site capabilities and establishes resource requirements.
2	QA Representative	The review of documentation to determine compliance with marketing authorization, The review of analytical method with QC to determine capability, equipment training requirements, The initiate conversion of donor site documentation into local system and format.
3	Production Representative	The review of process instructions/rules with process technologist to confirm capacity and capability, They consider any safety implications ex. Solvents, toxic and sanitizing materials, They consider impact on local standard operating procedures, Training requirement of supervisors and operators.
4	Engineering Representative	The review with production representative equipment and requirements, initiates required engineering modification change or part purchase, Reviews preventative maintenance and calibration impact. Ex. Use of more aggressive ingredients, temperature sensitive process ETC...
5	QC Representative	The review of analytical requirements, The availability with instruments, they are responsible for analytical method transfer for drug substances and drug product.

Table 1 : The Technology Transfer Team

APPLICATION OF TECHNOLOGY TRANSFER IN THE PHARMACEUTICAL INDUSTRY^[3]

- Formulation manufacturing process transfer.
- Analytical Method Transfer.
- Packaging Method Transfer.
- API Manufacturing Process Transfer.

WHEN DOES TECHNOLOGY TRANSFER OCCUR?^[3]

- The idea to Discovery lab.
- Discovery lab to Development lab.
- Development Lab to Kilo Lab.
- Kilo lab/Lab to Pilot Plant.
- Pilot Plant to Semi Works (Other Pilot Plant)
- Pilot Plant/Semi-Works to Manufacturing.
- Manufacturing to Manufacturing.

Plant: It is defined as a place where the 5M's, like material, money, man, method and machine, are brought together to manufacture the products.

Pilot Plant: It is part of the pharmaceutical industry where a lab-scale formula is transformed into a viable product by developing a liable and practical procedure of manufacture.

Scale-Up: The art of designing a prototype using the information obtained from the pilot plant model.^[4]

Importance Of Technology Transfer^[3, 6]

- Demonstration of the necessary information from research and development to Actual manufacturing.
- Demonstration of the necessary information on the existing product between various manufacturing places.
- Another importance is the smooth manufacturing of commercial products.

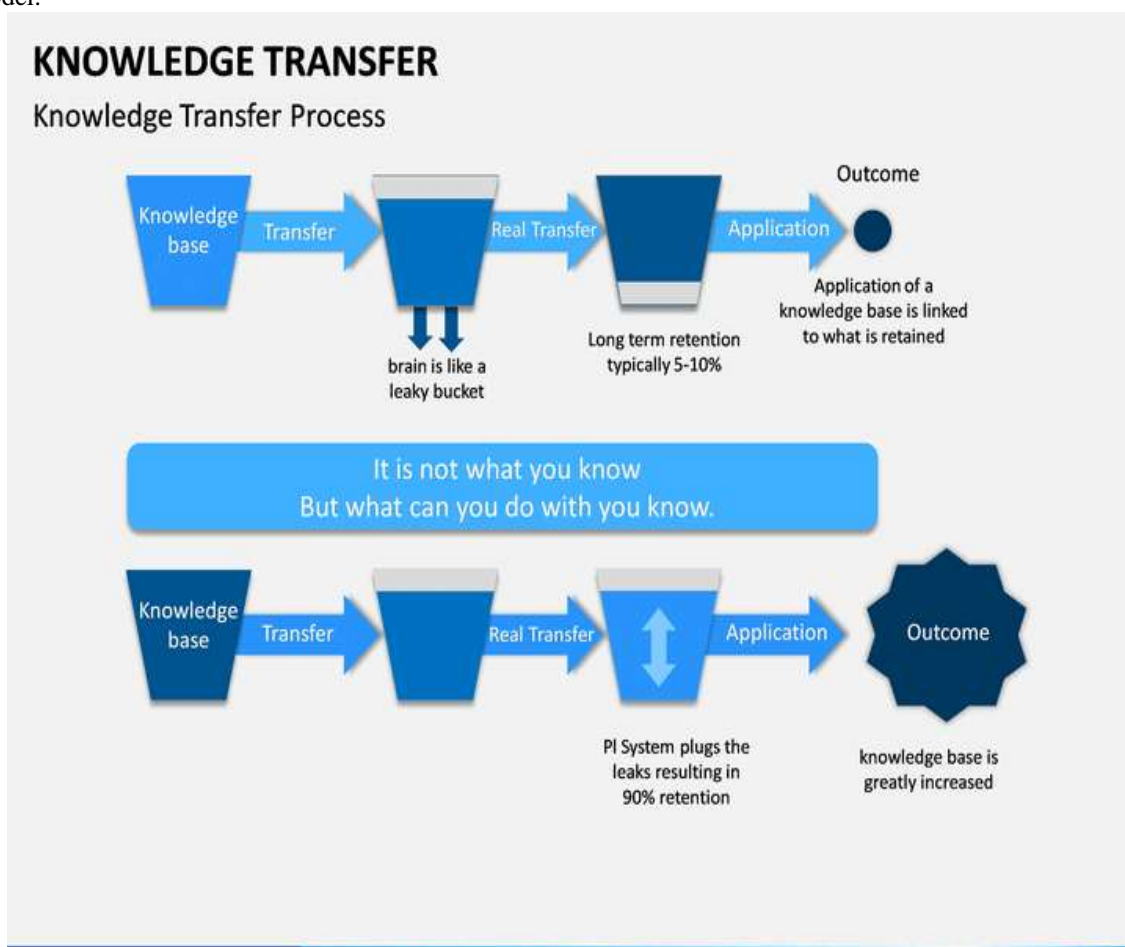


Fig. 2 : Knowledge Transfer Process

REASON FOR TECHNOLOGY TRANSFER^[3-14]

- Lack of manufacturing capacity.
- Lack of resources to launch the product commercially.
- Lack of marketing and distribution Capability.
- Exploitation in a different field of application.



<p>Team work, most and of the time..... Sending and Receiving Unit</p>	
	
<p>“Technology transfer is not a one way street”. The sending & receiving unit must be equally involved in the process to ensure success.</p>	<p>“You can tell Pharmacy finally that we have a product with three batches on predetermine specifications”</p>

Fig. 3: TT Process, Teamwork and Importance

FACTORS INFLUENCING TECHNOLOGY TRANSFER [3]

- Good business & manufacturing practices.
- Potential for competitive pricing.
- Strategic planning.
- Strong economy & environment.
- Transparent & efficient regulation.
- Opportunities for contingency supply.

AGENCIES FOR TECHNOLOGY TRANSFER IN INDIA

1 National Research Development Corporation (NRDC)

NRDC was founded in 1953 by Govt. of India to promote, develop and commercialize TT from the public to the private sector. NRDC transfers technologies, patents, inventions and methods derived by the national research and development institutions and universities underneath the directorial control of the Ministry of Science and Technology and the Department of Scientific and Industrial Research [1,7,8,9]

2 Asian and Pacific Centre for Transfer of Technology (APCTT)

APCTT is a United Nations Regional Institution governed by a Governing Council composed of a representative appointed by the Govt. of India. The bureau is under the Economic and Social Commission for Asia and the Pacific (ESCAP). APCTT was founded and established in 1977 in Bangalore. The main centre was changed to New

Delhi in 1993. It regulates the development projects which are sponsored internationally to supply more strength for TT in Asia and the Pacific.

APCTT control TT to and from small and medium-scale enterprises in Asia and the Pacific region. Technology transfer-related areas of APCTT are human resources development, institution building, studies, and business partnership development. [1,7,8,9]

3 Technology Information, Forecasting & Assessment Council (TIFAC)

TIFAC is an autonomous organization founded in 1988 under DST (Department of Science & Technology, Govt. of India). TIFAC is aimed to promote and support technology and innovations in selected areas of national importance. TIFAC concentrates on technology innovation and development through various sustained programs between industry and academia. TIFAC released its Vision 2020 under the leadership of Dr APJ Abdul Kalam, the former chairman of TIFAC in 16 technology areas and 2016 Vision 2035 prepared by TIFAC has been inaugurated by Hon'ble Prime Minister of India Shri. Narendra Modi in 12 thematic areas of national priorities and importance in Mysore, Karnataka. The 12 thematic areas are: [1,7,8,9]

- a) Education
- b) Medical Science and Health Care
- c) Food and Agriculture
- d) Water

- e) Energy
- f) Environment
- g) Habitat
- h) Transportation
- i) Infrastructure
- j) Manufacturing
- k) Materials
- l) Information and Communication Technologies (ICT).

4 Biotech Consortium India Limited (BCIL)

BCIL, a public limited company, was inaugurated in 1990 under the Indian Companies Act 1956. BCIL is promoted by the Dept. of Biotechnology (DBT), Ministry of Science and Technology, Govt. of India and All India Financial Institutions. BCIL was aimed at providing the necessary linkages among stakeholders and business support to accelerate the commercialization of biotechnology. BCIL assists scientists, technologies, research institutions, universities, first entrepreneurs, the corporate sector, national and international organizations, central Government, various state governments, banks and financial institutions. BCIL works in the following aspects: ^[1,7,8,9]

• Technology transfer • Project consultancy • Fund syndication • Information dissemination • Manpower training and placement related to biotechnology ^[1, 7, 8, 9]

5 Technology Bureau for Small Enterprises (TBSE)

TBSE provides the opportunity for small enterprises at the global level to the acquisition of technology or establishes business collaboration. TBSE works under the Development Commissioner, Ministry of Micro, Small and Medium Enterprises (MSME), and it is partially funded by the office of the Development Commissioner (DC), Small Scale Industries (SSI), and the Government of India. The critical features of TBSE are: ^[1,7,8,9]

- a) TBSE offers a professionally managed system for technology and collaboration search.
- b) TBSE builds up confidence between partners.
- c) TBSE has a proper mechanism for arranging technology and finance.
- d) TBSE provides a gateway to the global technology market through networking.
- e) TBSE takes up project appraisal and preparation of a business plan.

6 Small Industrial Development Bank of India (SIDBI)

SIDBI was established on April 2, 1990, through an Act of Parliament, under the Department of Financial Services, Government of India. It is a developed financial institution in India. The headquarter is situated in Lucknow, Uttar Pradesh. SIBI aims to provide refinance facilities and short-term lending to industries. It serves as the principal financial institution in the Micro, Small and Medium Enterprises sector (MSME). ^[1,7,8,9]

TECHNOLOGY TRANSFER-RELATED DOCUMENTS

1 Confidentiality Agreement

It is also called a non-disclosure agreement (NDA). It is used to protect the proprietary nature of the technology and retain the confidentiality of technology or invention. The drafting of the appropriate clauses can be essential for the maintenance of the value of the technology. This agreement is needed due to increased competition, and new technologies can be exploited. Thus, it is necessary to obtain protection for the continuous innovation process through confidentiality agreements. ^[1,7,8,9]

2 Licensing

The license agreement generally refers to licensing intellectual property rights such as; patents, trademarks, copyrights, etc. This agreement has a role in maintaining the confidentiality and secrecy aspects of the contract. ^[1,7,8,9]

3 MoUs

MoU stands for Memorandum of Understanding. It is a negotiated agreement and contract between the Government and the Management of the Central Public Sector Enterprise (CPSE). MoUs are used when the parties do not make an implicit legal commitment or cannot create a legally enforceable agreement. ^[1,7,8,9]

II. SUMMARY

The Summary is explained via the pasted image. The technology transfer method is completed after three validation batches by demonstrating the manufacturing process from R&D personnel to production personnel. Ensure the development team reliably transfers all relevant technical information to the receiving site. The method must Operate consistently, and the critical

process parameter must be well-defined and understood by the production or manufacturing personnel. It can be understood by the series of processes which are:^[11]

- a) Research & Discovery.
- b) Invent & disclose.
- c) Evaluate (patent Review Committee).
- d) Protect intellectual Property (IP).
- e) Market IP.
- f) Select a partner, Negotiate & License.
- g) Commercialize Products and Services.
- h) Benefit to society & Revenue.
- i) Distribute Revenue & Reinvest.

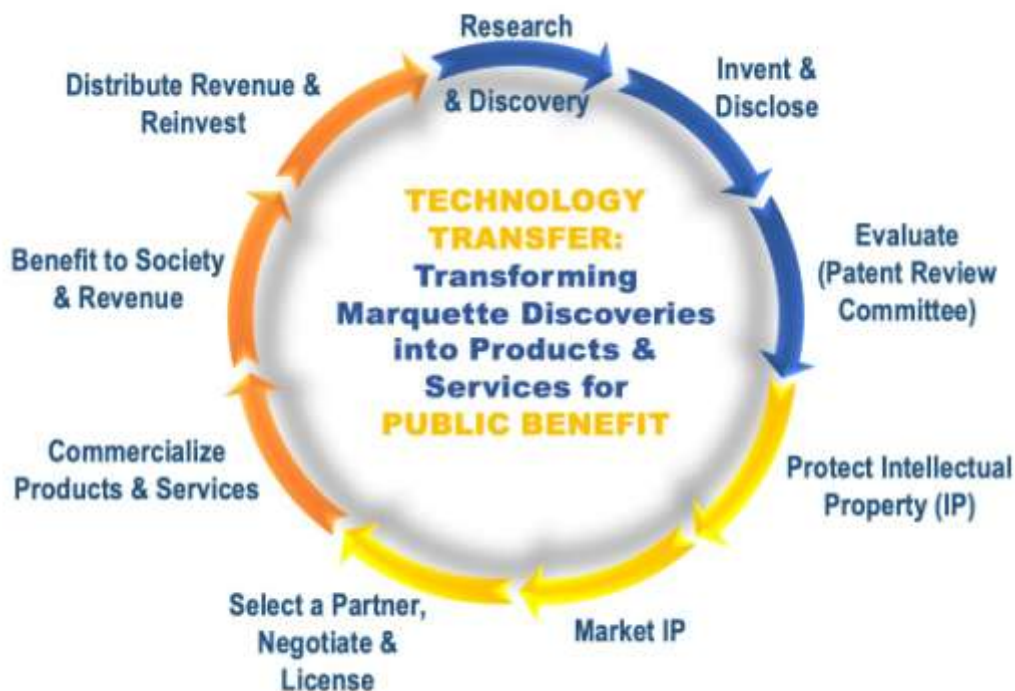


Fig. 4: Technology Transfer Model

III. CONCLUSIONS

- The transfer involves cost and expenditure negotiated and agreed upon by the transferee and transferor. The transfer may be successful if the transferee can utilize the technology for business gains and eventually assimilate it.
- The technology transfer team can achieve appropriate efficiency in technology transfer from development to commercialization through better communication and documentation. A cooperative effort by the crew results in more successful initial and consistent runs leading to an earlier license, earlier launch and a more significant marketshare.
- Enriched approaches like technology transfer to develop and start new production systems will enable pharmaceutical organizations to fully benefit from the recent improvements in new drug discovery and compete more effectively in a rapidly changing marketplace.

- A dedicated technology transfer organization is set up to facilitate and execute the process. Technology transfer can be successful if a receiving unit (RU) can routinely produce the transferred product, method or process against a predefined set of specifications agreed upon with a sending team (SU).
- Licensing is an imperative spectacle of Technology transfer that has gained momentum in the pharmaceutical industry by which pharmaceutical firms can contribute the research and development. Technology Transfer is a complex issue and should be dealt with holistically.

List of abbreviations:

1. TT: Technology Transfer.
2. R&D: Research and Development.
3. PDL: Process Development Lab.
4. F&D: Formulation and Development.
5. MS&T: Manufacturing Science and

- Technology.
6. QRM: Quality Risk Management.
 7. ICH: International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use.
 8. MOUs: Memorandum of Understandings

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